REMARKS

Upon entry of the present amendments, claims 1-33 will be pending. Claims 1-25 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 26, 27, 29, and 30 have been amended, and claims 31-33 have been added. The amendments and new claims find support in the specification at page 7, lines 5-9 and page 26, lines 1-3. Therefore, the amendments and new claims do not add new matter.

Restriction Requirement

Applicants affirm the election of Group II, drawn to claims 26-30, with traverse. The traversal is on the grounds that the Office Action has failed to show that the alleged groups are distinct.

The Action states, in pertinent part, that Groups I and II are distinct because the process of Group I could be practiced by another product, reciting "by hand" as an example of a materially different product and that the apparatus could be used for any method in which detection is performed with flow through cells, ranging from oligonucleotide synthesis to nucleic acid sequencing to detection by PCR.

First, Applicants respectfully submit that it is unlikely, if not impossible, to detect Raman signaling as claimed "by hand" at the nanoscale level (i.e., scale of single nucleotides). So, "by hand" does not exemplify a process using the product as claimed that can be practiced with another product. Second, it is not clear how Raman signaling as claimed (i.e., nanochannel or miocrochannel detection) would be used to detect oligonucleotide synthesis products, especially on the nanoscale level. Third, it is not clear why one would employ an apparatus that uses nanoscale detection of an object by Raman signaling if *detection* of the object has already been accomplished by PCR (i.e., "Further the apparatus can be used for any method in which detection is performed with flow through cells, ranging from oligonucleotides synthesis to . . . **detection by PCR**." Emphasis added.). These examples being eliminated, leaves only nucleic

acid sequencing, which is not a materially different process of using the product (i.e., apparatus) as claimed.

Because the Action has failed to provide an example supporting either or both of the necessary showings to establish that the alleged inventions are distinct, Applicants request that the restriction requirement be withdrawn and the alleged inventions rejoined.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 27, 29, and 30 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite.

Applicants traverse the rejection as it might apply to amended claims 27, 29, and 30. However, while Applicants do not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claims 27, 29, and 30 have been amended.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §102

Claims 26, 27, 29, and 30 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Su et al.

Applicants respectfully traverse the rejection against amended claims 26, 27, 29, and 30, including as it might be applied against new claims 31-33, for the reasons given below.

In pertinent part, the Office Action alleges that Su et al. teach all of the elements as recited in instant claims 26, 27, 29, and 30. However, Su et al. is silent with respect to channels comprising fixed nanoparticle aggregates.

Respectfully, review of Su et al. demonstrates that the apparatus therein reciting the use of nanoparticles, irrespective of whether nanoparticles are aggregated, require nanoparticles **to traverse** a flow-through cell for detection of nucleic acids (e.g., Examples 2 and 3, at pages 10 and 11 of the '240 application). Because Su et al. do not teach nanoparticles or nanoparticle aggregates fixed within a channel, the reference cannot teach an apparatus comprising

nanoparticle aggregates fixed within a channel. Thus, Su et al. do not anticipate the instant amended claims.

For these reasons, Applicants respectfully request that the rejection as applied against amended claims 26, 27, 29, and 30, including as it may be applied against new claims 31-33, be withdrawn.

Claims 26, 27, 29, and 30 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Shipwash.

Applicants respectfully traverse the rejection against amended claims 26, 27, 29, and 30, including as it might be applied against new claims 31-33, for the reasons given below.

The Office Action states, in pertinent part, that Shipwash teaches the elements as recited in the claims as filed, including a multiplicity of nanoparticles packed in the second channel (citing Fig. 14, paragraphs [0066], [0167], [0174], [0425], and Example 15). Further, the Action states that the apparatus of Shipwash is allegedly capable of detecting single nucleotides, citing paragraphs [0254] and [0255] for support.

Regarding the packed nanoparticles, Fig. 14 shows that particles are not packed in a second channel. In fact, paragraph [0425] (which is included in Example 15) states that the components flow past a detector, those components being the beads/nanoparticles and bound-sample. If the particles flow past the detector they cannot at the same time be packed[1] within a channel. The other paragraphs recited in the Action do not teach packed nanoparticles as alleged: i.e., [0066], describes nanoparticles and that reactions are carried out on the surface of such nanopartcles; [0167], provides a generalized discussion of microfluidics and microsystem fabrication; and [0174], discusses amino acid detection. Further, Shipwash is silent with respect to nanoparticle aggregates affixed within a channel, as the amended claims presently recite.

Regarding teaching of single nucleotides, review of the paragraphs recited, as well as the entire document, do not demonstrate that Shipwash teaches single nucleotide detection. Paragraphs [0254] and [0255] refer to immobilization of proteins and nucleic acids. Respectfully, based on the inventive concept of the reference (i.e., protein sequencing) and

[1] Based on the plain definition of "packed," flowing particles should not be interpreted to mean packed (e.g., to make into a compact bundle; to fill completely; to fill with packing, see < http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=packed&x=22&y=15>, last visited, October 17, 2005).

disclosures therein, immobilized nucleic acids refer to tRNAs, which are used to capture target single amino acids, not single nucleic acids. Thus, Shipwash neither teaches packed nanoparticles or affixed nanoparticle aggregates nor does Shipwash teach an apparatus that is capable of detecting single nucleotides.

For these reasons, Applicants respectfully request that the rejection against amended claims 26, 27, 29, and 30, including as it might be applied against new claims 31-33, be withdrawn.

Rejection Under 35 U.S.C. §103

Claims 26-30 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Dorre et al, in view of Dinh.

Applicants traverse the rejection, including as it may be applied to the new claims, for the reasons given below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation in the references themselves or in knowledge generally available to one of skill in the art, to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. And, finally the prior art reference (or references when combined) must teach all claim limitations. The teaching or suggestion and reasonable expectation of success must both be found in the prior art and not in Applicants' disclosure. (See MPEP §706.02(j)).

Respectfully, Applicants submit that the references when combined do not teach all claim limitations.

The Office Action alleges, in pertinent part, that Dorre et al. teach an apparatus comprising a reaction chamber; a first channel in fluid communications with the reaction chamber; a second channel; a multiplicity of nanoparticles packed in the second channel; and a detector coupled to the nanoparticle packed channel, citing section 2.3, pages 142-145, as support.

Section 2.3 describes the microstructures, including the labeled DNA immobilized on nanoparticles. However, the apparatus is described in Fig. 1 (page 140) and section 2.1. At page 140, column 2, the reference expressly recites:

> "With the help of an 'optical tweezer' (i.e. an IR trap laser focus [14, 15]), a loaded bead can be drawn into a capillary or microstructure channel and fixed there (See figure $1^{(1)}$). The sequential DNA degradation is started by the addition of reaction buffer and sequencing enzyme, i.e. 3'-5' exonuclease (figure $1^{(2)}$). Hydrolyzed monomers are transported by electro-osmotic flow and reach the second laser focus (figure $1^{(3)}$) where the fluorescent dyes are excited and emit a photon burst that is detected and analyzed with respect to its fluorescence characteristics."

Further, at page 150, column 1, the "trap focus" is defined as the place where exonuclease degradation occurs and the detection focus is where the monomers arrive according to their sequential order in the DNA fragment. Based on these passages, and Fig. 1, DNA-bound beads are immobilized in the microstructure channel where exonuclease degradation occurs. At best, this would be equivalent to the reaction chamber element of the instant claims. Further, the monomers are detected away from the immobilized beads (i.e., the detection focus of the reference), and thus, the beads are not operable coupled to a detector, whether or not such detector is a Raman detector or CCD. As such, and contrary to the allegations recited in the Action, the primary reference is deficient in that (1) there is no reaction chamber that is separate from a channel containing immobilized beads and (2) as the DNA-bound immobilized beads are contained within the reaction chamber, and released monomers are detected separately from the immobilized beads, there is no teaching of beads operably coupled to a Raman detector (or CCD).

The Action then offers Dinh to cure the deficiencies of Dorre et al. However, Dihn does not teach or suggest modifying the design of the Dorre et al. apparatus in which the immobilized beads contained in the channel where the reaction takes place be changed to the channel where detection takes place. Thus, Dinh does not cure the deficiencies of Dorre et al. because the combination does not achieve the instant invention as claimed.

Applicants submit that because the combined references do not teach all of the claim limitations, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the obviousness rejection be withdrawn as it may be applied to amended claims 26-30, and as it might be applied to new claims 31-33.

Rejection Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 26, 27, 29, and 30 stand provisionally rejected under the judicially created doctrine of obviousness double patenting allegedly over claims 24, 25, 27-30 of co-pending U.S. Application Ser. No. 10/299,287.

While not acquiescing to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, Applicants have provided herein a Terminal Disclaimer in compliance with 37 C.F.R. §1.321(c).

For this reason, Applicants respectfully request that the rejection against claims 26, 27, 29, and 30 be withdrawn.

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact the Applicants' undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge any fees, or credit any overpayments, to Deposit Account No. 07-1896.

Respectfully submitted,

Date: 12/9/05

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